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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,894	04/14/2006	Katsuyuki Hamada	TSU-007	4681

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,894	HAMADA ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/26/2007 and 07/06/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application 10/575,894 is a 371 of PCT/JP04/15221 filed on 10/15/2004, which claims the priority of JAPAN 2003-354983, filed on 10/15/2003.

Election/Restriction

1. Applicant's election of Group I, claims 1-3, 8, and 10, drawn to a cancer gene therapeutic drug including a carrier cell to be infected with an oncolytic virus, so as to make the oncolytic virus act on a tumor cell within a living body, wherein the carrier cell is selected from the group consisting of A549 cell, SW626 cell, and HT-3 cell, in the reply filed on 06/02/2008 is acknowledged. With regard to election of species, Applicant elected A549 cell (claim 1), 1A1.3B promoter (claim 2), and adenovirus (claims 3 and 10). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). In the reply filed on 06/02/2008, Applicant states that the Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution.

Claims 4-7 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3, 8 and 10 are currently under examination

Priority

2. This application 10/575,894 filed on 04/14/2006, the filed Oath and Declaration filed on 04/14/2006 claims benefit of foreign application Japan 2003-354983 filed on 10/15/2003. The Examiner acknowledges that Applicant has submitted on 04/14/2006 a certified copy of Japan 2003-354983 filed on 10/15/2003 under requirement of 35 U.S.C. 119 (a-d) conditions. However, it is noted that, the application Japan 2003-354983 filed on 10/15/2003 is in Japanese. Therefore, without a certified translation of Japan 2003-354983 filed on 10/15/2003, the effective filing date for the instant claims is the filing date of PCT/JP04/15521, 10/15/2004. Applicant cannot rely upon the foreign priority papers to overcome the rejection under 35 USC 102 (e) or 102 (a) as set forth below because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Objections

3. Claims 1-3, 8, and 10 are objected to because of the following informalities: It appears that the term "a cancer gene therapeutic drug" is meant to refer to "a composition comprising a carrier cell for gene therapy in treating cancer". However, as written, the term "cancer gene therapeutic drug" could read as a compound phase of "cancer gene" and "therapeutic drug". In this scenario, the recitation of "cancer gene" would need definition for clarity. It is advised that the term "a cancer gene therapeutic drug" should read "a composition comprising a carrier cell for gene therapy in treating cancer" or similarly appropriate language. Appropriate correction is required.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-3, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by **Hamada et al.** (Hamada et al., Identification of the human IAI.3B promoter element and its use in the construction of a replication-selective adenovirus for ovarian cancer therapy. *Cancer Res.* 63(10):2506-12, 2003; this reference is listed citation #1 on the IDS filed on 07/06/2008)

Claim interpretation: The preamble "A cancer gene therapeutic drug" recited in claim 1 is considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for limited patentable weight, if any. It is the composition of the claimed "cancer gene therapeutic drug" that imparts patentable weight for prior art rejection.

Hamada et al. disclosed the following teachings : **(i)** Identification of the promoter region of the IAI.3B gene and construction of a replication-selective adenovirus, AdE3-*IAI.3B*, driven by the promoter (See abstract and Figure 2, Hamada et al., 2003); **(ii)** The lung cancer A549 transfected with an oncolytic adenovirus Ad*E2F-1*^{RC}, and AdE3-*IAI.3B* has a construction

design similar to that of the adenovirus Ad*E2F-1*^{RC}, because both have an intact *E1A* promoter upstream of their respective heterologous promoters (See Discussion, second paragraph, right column, page 2510, Hamada, 2003), and **(iii)** AdE3-*IAI.3B* replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of ovarian cancer cells *in vitro*, in contrast, squamous cell carcinoma and normal cells were not able to support AdE3-*IAI.3B* replication (See abstract and Figure 3, Hamada et al., 2003), and **(iv)** In animal studies, AdE3-*IAI.3B* administered to flank and i.p. xenografts of ovarian cancer cells led to a significant therapeutic effect (See abstract and Figure 4, Hamada et al., 2003).

Thus, Hamada et al. (2003) clearly anticipates the claims 1-3 and 10 of instant invention.

5. Claims 1, 3, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by **Tsukuda et al.** (Tsukuda et al., An E2F-responsive replication-selective adenovirus targeted to the defective cell cycle in cancer cells: potent antitumoral efficacy but no toxicity to normal cell. *Cancer Res.* 62(12):3438-47, 2002; this reference is listed citation #5 on the IDS filed on 07/06/2008).

Claim interpretation: The preamble "A cancer gene therapeutic drug" recited in claim 1 is considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for limited patentable weight, if any. It is the composition of the claimed drug that imparts patentable weight for prior art rejection.

Tsukuda et al. disclosed the following teachings : **(i)** The construction of an adenovirus Ad*E2F-1*^{RC} and transfection of the Ad*E2F-1*^{RC} in A549 cells, so that E1A expression and viral

replication were under the control of the human E2F-1 promoter element (See abstract and Material and Methods, left column, page 3440, Tsukuda et al., 2002); **(ii)** The Ad*E2F-1*^{RC} virus replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of tumor cells (i.e. an oncolytic virus) *in vitro*, in contrast, non-proliferating normal epithelial, fibroblast, and endothelial cells, which express no E2F-1, were not able to support Ad*E2F-1*^{RC} replication (See abstract and Figures 3-5, Tsukuda et al., 2002); and **(iii)** In animal studies, different dosing regimens of Ad*E2F-1*^{RC} administered to flank xenografts of ovarian and lung cancers led to a significant therapeutic advantage often surpassing that seen in animals treated with the wild-type adenovirus (See abstract and Figures 6-7, Tsukuda et al., 2002).

Thus, Tsukuda et al. (2002) clearly anticipates the claims 1, 3, and 10 of instant invention.

6. Claims 1, 3, and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by **Li et al.** (US Patent 7,026,164, issued Apr. 11, 2006, file don 07/03/2003).

Claim interpretation: The preamble "A cancer gene therapeutic drug" recited in claim 1 is considered for limited patentable weight, if any. The intended use "for immunological treatment" recited in line 2 of claims 3 and 10 are considered for limited patentable weight, if any. It is the composition of the claimed drug that imparts patentable weight for prior art rejection.

Li et al. teaches adenovirus packing cell lines and the infection of 4 different oncolytic adenovirus (CG8900, CG8840, OV945 and OV1025) to A549 cell line, a lung cancer cell line (See abstract, bridging paragraph, columns 19-20, and Table 2, Li et al., 2006).

Thus, Li et al. (2006) clearly anticipates the claims 1, 3, and 10 of instant invention.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tsukuda et al.** (Tsukuda et al., An E2F-responsive replication-selective adenovirus targeted to the defective cell cycle in cancer cells: potent antitumoral efficacy but no toxicity to normal cell. *Cancer Res.* 62(12):3438-47, 2002; this reference is listed citation #5 on the IDS filed on 07/06/2008) in view of **Molnar-Kimber et al.** (Molnar-Kimber et al., WO 99/45783, international publication date, 09/16/1999; this reference is listed on the IDS filed on 03/26/2007).

Claim interpretation: The preamble "A cancer gene therapeutic drug" recited in claim 1 is considered for limited patentable weight, if any. It is the composition of the claimed drug that imparts patentable weight for prior art rejection.

Tsukuda et al. disclosed the following teachings : **(i)** The construction of an adenovirus Ad*E2F-1*^{RC} and transfection of the Ad*E2F-1*^{RC} in A549 cells, so that E1A expression and viral replication were under the control of the human E2F-1 promoter element (See abstract and

Material and Methods, left column, page 3440, Tsukuda et al., 2002); **(ii)** The Ad*E2F-1*^{RC} virus replicated as efficiently as the wild-type adenovirus and caused extensive cell killing in a panel of tumor cells (i.e. an oncolytic virus) *in vitro*, in contrast, non-proliferating normal epithelial, fibroblast, and endothelial cells, which express no E2F-1, were not able to support Ad*E2F-1*^{RC} replication (See abstract and Figures 3-5, Tsukuda et al., 2002); and **(iii)** In animal studies, different dosing regimens of Ad*E2F-1*^{RC} administered to flank xenografts of ovarian and lung cancers led to a significant therapeutic advantage often surpassing that seen in animals treated with the wild-type adenovirus (See abstract and Figures 6-7, Tsukuda et al., 2002).

Tsukuda et al. do not teach the limitation "furthering comprising a tumor cell to be administered for tumor vaccination" as recited in claim 8 of instant application.

However, Molnar-Kimber et al. teaches the following: (i) A producer cell (i.e. a tumor cell line for viral packaging) comprises an oncolytic adenovirus which is capable of replicating in the producer cell and methods of using these producer cells to treat a subject having tumor cells and making a medicament for use in such treatment (See abstract, third paragraph, page 7, Molnar-Kimber et al., WO 99/45783) , and (ii) A producer cell (i.e. a tumor cell line for viral packaging) may also be rendered incapable of sustained survival in the body of the patient by exposing the producer cell to a lethal dose of radiation prior to providing the producer cell to the subject, and formation of a producer cell-tumor cell complex may generate or expose antigenic regions which can be recognized by the subject's immune system, leading to generation of an immune response against the tumor cells (See lines 5-8, 28-30, page 13, Molnar-Kimber et al., WO 99/45783).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Tsukuda et al. regarding administration of A459 cells infected with oncolytic adnovirus Ad*E2F-1*^{RC} to animals for cancer treatment with the teachings of Molnar-Kimber et al. regarding a radiated producer cell (i.e. a tumor cell line for viral packaging) infected with oncolytic adenovirus forming a complex with tumor cell complex that can leads to generation of an immune response against the tumor cells, to arrive at a composition including A549 cell infected with an oncolytic adenovirus and further comprising a tumor cell to be administered for tumor vaccination, as recited in claim 8 of instant application.

One having ordinary skill in the art would have been motivated to combine the teachings of Tsukuda et al. and Molnar-Kimber et al. because there are two different molecular mechanisms involved in treating cancer by a producer/packing cell line infected with an oncolytic adenovirus. The administration of non-radiated A459 cells infected with mutated oncolytic adenovirus Ad*E2F-1*^{RC} taught by Tsukuda et al. results to killing of cancer cells, and the administration of radiated producer cell (i.e. a tumor cell line for viral packaging) infected with oncolytic adenovirus forming a complex with tumor cell complex, taught by Molnar-Kimber et al., can generate an immune response against the tumor cells.

There would have been a reasonable expectation of success given (i) successful demonstration of treating cancer cells A459 cells infected with replication-selective oncolytic adenovirus Ad*E2F-1*^{RC} leads to potent anti-tumoral efficacy but no toxicity to normal cells by the teachings of Tsukuda et al. and (ii) the immune response against cancer cells elicited by the administration of radiated producer cell infected with oncolytic adenovirus by the teachings of Molnar-Kimber et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

8. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Wu-Cheng Winston Shen, Ph. D.

Patent Examiner

Art Unit 1632

/Peter Paras, Jr./

Supervisory Patent Examiner, Art Unit 1632